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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,138	08/28/2000	Shigeru Kinoshita	KINOSHITA3	9673

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EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/23/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/623,138	KINOSHITA, SHIGERU	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vitamin D compounds disclosed in specification page 4, lines 6-21, does not reasonably provide enablement for other vitamin D compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define "active vitamin D compounds" or "derivatives or analog of vitamin D_3". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "active vitamin D compounds" or "derivatives or analog of vitamin D_3" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all "active vitamin D compounds" or "derivatives or analog of vitamin D_3", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-13, and 15-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "active vitamin D" in claims 1 and 11 renders the claims indefinite as to the compounds the claims encompassed thereby.

The phrase "derivative or analog of active vitamin D" in claims 2 and 12 renders the claims indefinite as to the compounds the claims encompassed thereby.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Itoh et al. (WO96/29079, the English translation, Patent US 6,248,732, is also provided).

Itoh et al. teaches an ophthalmic composition comprising calcitriol (See particularly col. 11, line 5-10). Please note that the recitation of the intended use of the compound (e.g., as a Langerhans cells migration inhibitor) does not lend patentable weight to claims drawn to a composition.

Applicants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation for such utility. In the instant application, as in *Ex parte Novitski*, supra, the claims are directed to treating or preventing ocular inflammatory disease with old and well known compounds or compositions, i.e., the method steps comprise administering the active vitamin D compound to a mammal. It is now well settled law that administering

compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from anticipated utilities with specification limitations will not be successful. At page 1391, *Ex parte Novitski*, supra, the Board said "We are mindful that, during the patent examination, pending claims must be interpreted as broadly as their terms reasonably allow. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). As often stated by the CCPA, "we will not read into claims in pending applications limitations from the specification." *In re Winkhaus*, 52 F.2d 637, 188 USPQ 219 (CCPA 1975).". In the instant application, Applicants' failure to distance the proffered claims from the anticipated treatment and prophylactic utility, renders such claims anticipated by the prior inherent use. Please see Itoh et al. col. 12, line 59-67.

Claims 1-20 rejected under 35 U.S.C. 102(e) as being anticipated by Itoh et al. (US Patent 5,876,709).

Itoh'709 teaches an ophthalmic composition comprising calcitriol (See particularly col. 15, line 65- col. 16, line 4; Example 2; col. 16, line 49-67 to col. 17, line 1-4; Examples 8 and 9). Please note that the recitation of the intended use of the compound (e.g., as a Langerhans cells migration inhibitor) does not lend patentable weight to claims drawn to a composition.

Itoh'709 further teaches the administration of calcitriol as ophthalmic preparation to guinea pigs (See particularly ocl. 18, 65- col.19, lines 67; Test Example 3). The

method of treating or preventing ocular inflammatory disease herein are anticipated by Itoh'709's teaching because Itoh'709 inherently teaches the method steps herein. See *Ex parte Novitski*, supra.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dam et al. (Journal of Investigational Dermatology Symposium proceedings; 1996;1(1):72-77) in view of Itoh et al. (WO96/29079, the English translation, Patent US 6,248,732, is also provided), Hingorani et al. (Drugs 1995; 50(2); 208-221), and Muller et al. (Journal of Investigational Dermatology Symposium proceedings; 1996;1(1): 68-71).

Dam et al. teaches calcitriol and calcipotriol are useful to suppress the number of Langerhans cells (LC) when applied topically (See particularly page 72, col. 2, last paragraph). Dam et al. also teaches calcitriol or calcipotriol inhibit THF-α, a factor which can induce migration of LC (See page 76, col. 1, 2md paragraph). Dam et al. also teaches calcitriol and calcipotriol suppress the T-cell proliferation (See page 75, col. 2, first paragraph).

Dam et al. does not teach calcitriol is in a form of ophthalmic solution. Dam et al. does not expressly teach calcitriol is useful in treating keratoconjuctivitis and preventing phlyctenular keratitis or corneal infiltration. Dam et al. does not expressly teach calcitriol is useful in a method to inhibit interleukin-1 production in cornea epithelium.

Itoh et al. teaches that calcitriol can be formulated into an ophthalmic composition (See See particularly col. 11, line 5-10).

Hingorani et al. teaches atopic keratoconjunctivitis is a T-cell inflammation prominent disorder (See particularly abstract). Hingorani et al. also teaches atopic keratoconjunctivitis may lead to infiltration and corneal involvement such as epithelial keratitis (See particularly page 210, col. 1, last paragraph).

Muller et al. teaches the calcitriol inhibits the production of interleukin-1 at a presecretory level such as reducing the levels of interleukin-1α mRNA (See page 68, col.2, third paragraph).

It would have been obvious to one skill in the art when the invention was made to employ calcitriol, in ophthalmic solution dosage form, in a method to treat keratoconjuctivitis and prevent phlyctenular keratitis or corneal infiltration. It would have been obvious to one skill in the art when the invention was made to employ calcitriol in a method to inhibit interleukin-1 production in cornea epithelium.

One of ordinary skill in the art would have motivated to employ calcitriol, in ophthalmic solution dosage form, in a method to treat keratoconjuctivitis and prevent phlyctenular keratitis or corneal infiltration because it is known that atopic keratoconjunctivitis is a T-cell inflammation prominent disorder and may lead to

infiltration and corneal involvement such as epithelial keratitis. Therefore, employing any T-cell proliferation inhibitors, including calcitriol would have been reasonably expected to treat keratoconjunctivitis and prevent keratitis including phlyctenular keratitis or corneal infiltration thereby. Furthermore, One of ordinary skill in the art would have motivated to employ calcitriol in a method to inhibit interleukin-1 production in cornea epithelium because calcitriol is known to inhibit the production of interleukin-1α at a presecretory level by reducing the level of interleukin-1α mRNA. One of ordinary skill in the art would therefore reasonably expect calcitriol be useful in inhibiting the production of interleukin-1 regardless of whether the interleukin-1 is secreted by corneal epithelium or not.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
November 18, 2001

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
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